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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,350	07/11/2003	Ranga R. Namburi	27493U	2736

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NATH & ASSOCIATES
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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/617,350	NAMBURI ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *9-13 and 24-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 14-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS 1-41 ARE PRESENTED FOR EXAMINATION

Applicant's election ***with*** traverse of Group I (claims 1-27) in the reply filed on 4/27/2007 is acknowledged. The traversal is on the ground(s) that to examine Groups I-III together would not present "serious burden" under MPEP § 803. This is not found persuasive because the inventions are independent or distinct **and** there would be a serious search burden if they were to be examined together. For example, the particles claimed in Group II (claims 28-38) recite limitations not present or required in the process of Group I. As such, it is very clear that a search of Group I would not result in identification of the particular limitations recited in the claims of Group II. Further, searching the process of Group I would not uncover methods of treating "a disorder" comprising administering an oral dosage form according to claim 34, which requires the limitations of the specific particles of Group II. With respect to Applicants' argument that they have paid a filing fee for an examination of all the claims in this application, as set forth in the Restriction Requirement mailed 3/27/2007 and discussed *supra*, the present application contains patentably distinct inventions that would present an undue search burden on the Examiner if they were to be examined together.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 28-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/27/2007.

Applicants' election of the species "ketoconazole" in the reply filed on 4/27/2007 is acknowledged. Because Applicants did not distinctly and specifically point out the supposed

errors in the species election requirement, the election has been treated as an election **without** traverse (MPEP § 818.03(a)).

Claims 9-13 and 24-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/27/2007.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. § 119(e) or under 35 U.S.C. § 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120 as follows:

The later-filed application must be an application for a patent for an invention, which is also disclosed, in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/933,032, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. For example, the disclosure of the '032 application does not provide support for the instantly claimed method of manufacturing an active oral dosage form because it does not disclose methods wherein the single phase working solution contains

acetone. The methods of the '032 application comprise dissolving into solvent systems of aqueous alcohol and water and strong acid. Further, the methods of the '032 application disclose only methods of preparing particles containing itraconazole.

Support for the instantly claimed invention was found in U.S. Provisional Application No. 60/401,121, filed August 5, 2002 (*e.g.*, claims 1, 3-6, 8-10 and 13-18). Accordingly, the earliest effective U.S. filing date afforded the instant claims is 8/5/2002.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statements filed 11/10/2003 and 12/22/2003. The Examiner has considered the references cited therein to the extent that each is a proper citation. The International Search Report for PCT/NL03/00563 (reference 5 in the IDS filed 12/22/2003) was not considered because International Search Reports are not considered "published" articles by the USPTO. Please see the attached USPTO Form 1449.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 recites the limitation "said surfactant" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 17 depends from claim 1. Claim 1 does not recite that a surfactant is used in the claimed method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1-8, 14-16 and 18-23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gilis *et al.* (WO 00/03697; Published Jan. 27, 2000) (cited by Applicants in IDS filed 12/22/2003) and Ishibashi *et al.* (U.S. Patent Application Publication No. US 2003/0012815 A1 (Published Jan. 16, 2003; Filed Jan. 26, 2001) (newly cited art) in view of Mathir *et al.* (Journal of Microencapsulation, 1997, vol. 14, pages 743-751) (cited by Applicants in IDS filed 12/22/2003).

The instant claims recite a method of manufacturing an active agent dosing form. Said method comprises a single working solution of active agent, water, a water-soluble polymer and a solvent, wherein the solvent is selected from an alcohol, acetone and mixture thereof. The working solution is combined with core particles to produce active agent coated particles.

Gilis *et al.* disclose pellets having a core coated with an antifungal and a polymer (Abstract). With respect to solvents used in forming coated core particles, the reference discloses that dichloromethane and methanol are both Class 2 solvents whose presence in pharmaceutical products should be limited (page 2, lines 28-30). Specifically, the pellets disclosed in Gilis *et al.* comprise: a) a central, rounded or spherical core having a diameter of about 710-1190 μM); b) a coating film of a water-soluble polymer and an antifungal agent; and c) a seal-coating polymer layer, characterized in that the residual solvent levels in said pellets is within limits set by the ICH, that is, the concentration of dichloromethane is less than 600 ppm, most preferably less than 250 ppm (page 4, lines 24-32). Accordingly, Gilis *et al.* disclose using ethanol as an alcoholic co-solvent that is necessary for applying the drug coat layer to the cores (page 4, lines 34-35), thus meeting the limitations of claim 15. Water-soluble polymers include those recited in instant claim 16, for example, hydroxypropyl methylcellulose, polyvinylpyrrolidones and methacrylates (page 6, line 23 to page 7, line 3). Such polymers are disclosed to have an apparent viscosity of 1 to 100 mPa.s when dissolved in a 2% aqueous solution, thus reasonably encompassing the limitations of instant claim 4 (page 5, lines 32-34). With respect to the composition of the core particles recited in instant claims 18-19, Gilis *et al.* disclose identical core particles composed of, for example, mannitol or microcrystalline cellulose (page 5, lines 8-19). Preferred antifungal agents for use as drugs in the drug-coating layer are lipophilic azole antifungals, in particular itraconazole (page 7, lines 10-11). The instantly claimed weight ratio of active agent to polymer is obviated by those disclosed at page 7, lines 15-30, for example, 1:1 to 1:5. With respect to the limitations of instant claim 22 wherein an external coating is applied to the drug coated spheres, Gilis *et al.* disclose such an external

coating at page 8, lines 28-32. The addition of surfactants as recited in instant claim 3 is disclosed at page 9, lines 1-4. A drying step as recited in claim 1 is disclosed at page 10, lines 32-38).

The reference thus clearly suggests a process of forming drug-coated particles comprising the same steps as those instantly claimed. Further, Gilis *et al.* suggest that the dichloromethane content of the coating should be limited. As such, Gilis *et al.* provide the motivation to use a solvent other than dichloromethane to formulate a coating solution for coating core particles. Gilis *et al.* differ from the claims with respect to the solvents used in the coating solution.

Ishibashi *et al.* disclose drug-containing core substance having a multi-layered coating layer (Abstract). With respect to the coating solution used to coat the disclosed core particles, the reference discloses that the solvent system should dissolve both the hydrophobic organic compound and water-soluble polymer (page 6, ¶ [0057]). Suitable solvents include alcohols such as ethanol as well as ketones such as acetone (*id.*).

Mathir *et al.* provide further motivation to use aqueous-based coating solutions in the formation of coated particles. For example, at page 744, the reference discloses that aqueous coating systems offer a safer, more economic and environmentally friendly alternative to organic-based coating systems.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use any suitable solvent system, especially an aqueous-based solvent system, to provide a working solution for coating core particles. In the instant case, the skilled artisan would have been imbued with at least a reasonable expectation that a solvent system consisting of alcohol, acetone or mixtures thereof would be effective in dissolving both a water-soluble

polymer as well as a hydrophobic active agent such as ketoconazole. The Examiner also notes that acetone is well known in the art as an organic solvent suitable for dissolution of organic compounds. Further, coating core particles with an active agent is a well-known process as evidenced by the cited references. Applicants' process of coating such particles differs from the prior art in the composition of the working solution. However, as discussed *supra*, modifying said working solution so as to provide dissolution of both a hydrophobic active agent and a water-soluble polymer would require nothing more than identification of solvents suitable for such purpose. To this point, Ishibashi *et al.* disclose that acetone and ethanol are solvents that may effectively dissolve both hydrophobic organic compounds and water-soluble polymers. Gilis *et al.* provide the motivation to use a solvent other than dichloromethane wherein they disclose that the dichloromethane content of the coating should be limited. Mathir *et al.* provide further motivation to use aqueous-based coating systems wherein they disclose that such systems are safe and more environmentally friendly than organic-based coating systems.

With respect to instant claim 2, which recites that the pH of the working solution is adjusted to solubilize the active agent, such a method step would have been obvious to the skilled artisan. For example, many drugs have pH-dependent solubility. As such, if the drug being dissolved in the working solution is insoluble at the pH of the solution, the skilled artisan would be motivated to adjust the pH so as to fully solubilize the active agent.

With respect to instant claim 6, which recites specific ratios of water to working solution, it is well within the level of ordinary skill in the art to determine optimal working ranges of prior art processes and compositions. As such, because an aqueous-based coating solution is prima facie obvious as discussed supra, determining the optimum ratio of water to, for example,

ethanol or acetone in such coating solutions, would require nothing more than routine optimization.

Accordingly, the claims are deemed properly rejected as being obvious over Gilis *et al.* and Ishibashi *et al.* in view of Mathir *et al.* who provide the teaching, suggestion and motivation to use any suitable solvent system in order to provide a working solution for coating core particles.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Patent Examiner
AU 1614

July 19, 2007

PHYLLIS SPIVACK
PRIMARY EXAMINER

7/20/07